

REMARKS

This paper is filed in response to the Communication dated June 26, 2008, stating that Applicants' response filed on March 4, 2008 was not fully responsive to the prior Office Action. Specifically, the Communication states that in the Amendment and Reply filed on March 4, Applicants amended claim 11 to recite a Markush group of tissue-specific inflammatory disorders. According to the Examiner, it is unclear which of the disorders correspond to the elected species of "inflammatory bowel disease."

Amended claim 11 recites the following Markush group of tissue-specific inflammatory disorders:

the tissue-specific inflammatory disorder is selected from the group consisting of adrenalitis, alveolitis, angiocholecystitis, appendicitis, balanitis, blepharitis, bronchitis, bursitis, carditis, cellulitis, cervicitis, cholecystitis, chorditis, cochlitis, colitis, conjunctivitis, cystitis, dermatitis, diverticulitis, encephalitis, endocarditis, esophagitis, eustachitis, fibrositis, folliculitis, gastritis, gastroenteritis, gingivitis, glossitis, hepatosplenitis, keratitis, labyrinthitis, laryngitis, lymphangitis, mastitis, media otitis, meningitis, metritis, mucitis, myocarditis, myositis, myringitis, nephritis, neuritis, orchitis, osteochondritis, otitis, pericarditis, peritendonitis, peritonitis, pharyngitis, phlebitis, poliomyelitis, prostatitis, pulpitis, retinitis, rhinitis, salpingitis, scleritis, sclerochoroiditis, scrotitis, sinusitis, spondylitis, steatitis, stomatitis, synovitis, syringitis, tendonitis, tonsillitis, urethritis, and vaginitis.

Inflammatory bowel disease (IBD) is a group of inflammatory conditions of the large http://en.wikipedia.org/wiki/Colon_anatomy intestine and, in some cases, the small intestine. See the definition of Inflammatory Bowel Disease provided by Wikipedia, http://en.wikipedia.org/wiki/Inflammatory_bowel_disease, accessed on August 7, 2008, a copy of which is attached. IBD includes conditions such as Crohn's disease, ulcerative colitis, collagenous colitis, lymphocytic colitis, ischaemic colitis, diversion colitis, Behçet's syndrome, infective colitis, and indeterminate colitis. *Id.*

Thus, amended claim 11 reads on the elected species of "inflammatory bowel disease", and examples of IBD conditions specifically recited in claim 11 include, but are not limited to, colitis.

CONCLUSION

Applicants believe that the present application is now in condition for allowance.
Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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By M. M. Simkin

FOLEY & LARDNER LLP
Washington Harbour
3000 K Street NW, Suite 500
Washington, D.C. 20007-5143
Telephone: (202) 672-5538
Facsimile: (202) 672-5399

Michele M. Simkin
Attorney for Applicants
Registration No. 34,717

Inflammatory bowel disease

From Wikipedia, the free encyclopedia

Not to be confused with irritable bowel syndrome.

In medicine, **inflammatory bowel disease (IBD)** is a group of inflammatory conditions of the large intestine and, in some cases, the small intestine.

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| Inflammatory bowel disease <i>Classification and external resources</i> | |
|---|---|
| DiseasesDB | 31127 (http://www.diseasesdatabase.com/ddb31127.htm) |
| eMedicine | med/1169 (http://www.emedicine.com/med/topic1169.htm) emerg/106 (http://www.emedicine.com/emerg/topic106.htm) oph/520 (http://www.emedicine.com/oph/topic520.htm) |
| MeSH | D015212 (http://www.nlm.nih.gov/cgi/mesh/2008/MB_cgi?field=uid&term=D015212) |

Forms

The main forms of IBD are Crohn's disease and ulcerative colitis (UC).

Accounting for far fewer cases are other forms of IBD:

- Collagenous colitis
- Lymphocytic colitis
- Ischaemic colitis
- Diversion colitis
- Behget's syndrome
- Infective colitis
- Indeterminate colitis

The main difference between Crohn's disease and UC is the *location and nature* of the inflammatory changes. Crohn's can affect any part of the gastrointestinal tract, from mouth to anus (*skip lesions*), although a majority of the cases start in the terminal ileum. Ulcerative colitis, in contrast, is restricted to the colon and the rectum. [1] (<http://www.ccfa.org/>)

Microscopically, ulcerative colitis is restricted to the mucosa (epithelial lining of the gut), while Crohn's disease affects the whole bowel wall.

Finally, Crohn's disease and ulcerative colitis present with extra-intestinal manifestations (such as liver problems, arthritis, skin manifestations and eye problems) in different proportions.

Rarely, a definitive diagnosis of either Crohn's disease nor ulcerative colitis can be made because of idiosyncrasies in the presentation. In this case, a diagnosis of indeterminate colitis may be made. Although a recognised definition, not all centres refer to this.

Symptoms and diagnosis

Although very different diseases, both may present with any of the following symptoms: abdominal pain, vomiting, diarrhea, hematochezia (bright red blood in stools), weight loss and various associated complaints or diseases like arthritis, pyoderma gangrenosum, and primary sclerosing cholangitis. Diagnosis is generally by colonoscopy with biopsy of pathological lesions.

Treatment

Depending on the level of severity, IBD may require immunosuppression to control the symptom, such as prednisone, infliximab (Remicade), azathioprine (Imuran), methotrexate, or 6-mercaptopurine. More commonly, treatment of IBD requires a form of mesalamine. Often, steroids are used to control disease flares and were once acceptable as a maintenance drug. In use for several years in Crohn's disease patients and recently in patients with Ulcerative Colitis, biologicals has been used such as the intravenously administered Remicade. Severe cases may require surgery, such as bowel resection, strictureplasty or a temporary or permanent colostomy or ileostomy. Alternative medicine treatments for bowel disease exist in various forms, however such methods concentrate on controlling underlying pathology in order to avoid prolonged steroid exposure or surgical excision[2]

(http://www.gaiagarden.com/articles/therapeuticapplications/ta_treating_bowel_disease.)

Usually the treatment is started by administering drugs with high anti-inflammatory affects, such as prednisone. Once the inflammation is successfully controlled, the patient is usually switched to a lighter drug to keep the disease in remission, such as Asacol, a mesalamine. If unsuccessful, a combination of the aforementioned immunosuppression drugs with a mesalamine (which may also have an anti-inflammatory effect) may or may not be administered, depending on the patient.

Prognosis

While IBD can limit quality of life because of pain, vomiting, diarrhea, and other socially unacceptable symptoms, it is rarely fatal on its own. Fatalities due to complications such as toxic megacolon, bowel perforation and surgical complications are also rare.

While patients of IBD do have an increased risk of colorectal cancer this is usually caught much earlier than the general population in routine surveillance of the colon by colonoscopy, and therefore patients are much more likely to survive.

The goal of treatment is toward achieving remission, after which the patient is usually switched to a lighter drug with fewer potential side effects. Every so often an acute resurgence of the original symptoms may appear: this is known as a "flare-up". Depending on the circumstances, it may go away on its own or require medication. The time between flare-ups may be anywhere from weeks to years, and varies wildly between patients - a few have never experienced a flare-up.

Recent findings

A recent hypothesis posits that some IBD cases are caused by an overactive immune system attacking various tissues of the digestive tract because of the lack of traditional targets such as parasites and worms. The number of people being diagnosed with IBD has increased as the number of infections by parasites, such as roundworm, hookworm and human whipworms, has fallen, and the condition is still rare in countries where parasitic infections are common. This is similar to the hygiene hypothesis applied to allergies.

Initial reports (Summers *et al* 2003) suggest that "helminthic therapy" may not only prevent but even cure (or control) IBD: a drink with roughly 2,500 ova of the *Trichuris suis* helminth taken twice monthly decreased symptoms markedly in many patients. It is even speculated that an effective "immunization" procedure could be developed—by ingesting the cocktail at an early age.

Prebiotics and probiotics are showing increasing promise as treatments for IBD (Furrie, 2005) and in some studies have proven to be as effective as prescription drugs (Kruis, 2004).

More recently, research (Hue *et al* 2006) has shown that IL-23 is overexpressed in tissues taken from Mouse models of IBD. The group showed that knocking out IL-23 (heterodimer of IL-12p40 and IL-23p19) severely reduced inflammation of the bowel, both in terms of cells and proinflammatory cytokine production. Also, they found that a novel group of CD4⁺ T lymphocytes, Th17 T cells, are highly upregulated in bowels of diseased mice. Taken together, the group shows that IL-23 but not IL-12 (IL-12p40 and IL-12p35; share a subunit) drives innate and T cell mediated intestinal inflammation.

In 2005 New Scientist published a joint study by Bristol University and Bath University on the apparent healing power of cannabis on IBD. Reports that cannabis eased IBD symptoms indicated the possible existence of cannabinoid receptors in the intestinal lining, which respond to molecules in the plant-derived chemicals. CB1 cannabinoid receptors – which are known to be present in the brain – exist in the endothelial cells which line the gut, it is thought that they are involved in repairing the lining of the gut when damaged. The team deliberately damaged the cells to cause inflammation of the gut lining and then added synthetically produced cannabinoids; the result was that gut started to heal: the broken cells were repaired and brought back closer together to mend the tears. It is believed that in a healthy gut, natural endogenous cannabinoids

are released from endothelial cells when they are injured, which then bind to the CB1 receptors. The process appears to set off a wound-healing reaction, and when people use cannabis, the cannabinoids bind to these receptors in the same way. Previous studies have shown that CB1 receptors located on the nerve cells in the gut respond to cannabinoids by slowing gut motility, therefore reducing the painful muscle contractions associated with diarrhoea. The team also discovered another cannabinoid receptor, CB2, in the guts of IBD sufferers, which was not present in healthy guts. These receptors, which also respond to chemicals in cannabis, appear to be associated with apoptosis – programmed cell death – and may have a role in suppressing the overactive immune system and reducing inflammation by mopping up excess cells.^[1]

References

1. ^ Wright K, et al. Differential Expression of Cannabinoid Receptors in the Human Colon: Cannabinoids Promote Epithelial Wound Healing. *Gastroenterology*, Volume 129, Issue 2, Pages 437 - 453
- Furrie, E. Biotic Therapy Cuts Inflammation in Ulcerative Colitis. *Gut* 2005;54:242-249.
- Kruis, W., P Fric, J Pokrotnieks, M Lukás, B Fixa, M Kascák, M A Kamm, J Weismueller, C Beglinger, M Stolte, C Wolff, and J Schulze. Maintaining remission of ulcerative colitis with the probiotic *Escherichia coli* Nissle 1917 is as effective as with standard mesalazine. *Gut* 2004; 53: 1617-1623.
- Summers RW, Elliott DE, Qadir K, Urban JF Jr, Thompson R, Weinstock JV. *Trichuris suis seems to be safe and possibly effective in the treatment of inflammatory bowel disease*. *Am J Gastroenterol* 2003;98:2034-41. PMID 14499784 (<http://www.ncbi.nlm.nih.gov/pubmed/14499784>).
- Hue S, Ahern P, Buonocore S, Kullberg MC, Cua DJ, McKenzie BS, Powrie F, Maloy KJ. Interleukin-23 drives innate and T cell-mediated intestinal inflammation. *J. Exp. Med.* 2006; **203**:2473-2483. [3] (<http://www.jem.org/cgi/content/abstract/203/11/2473>)
- Wright K, et al. Differential Expression of Cannabinoid Receptors in the Human Colon: Cannabinoids Promote Epithelial Wound Healing. *Gastroenterology*, Volume 129, Issue 2, Pages 437 - 453

External links

- Information about IBD (<http://www.ccfa.org/info/?LMI=4>) from the Crohn's and Colitis Foundation of America
- European Federation of Crohns and Colitis Associations (<http://www.efcca.org/>)
- IBDCure International (<http://www.ibdcure.org/IBD/>)
- Frequently Asked Questions about IBD in Children (<http://ibdkids.unc.edu/index.php/TopMenu/FAQ>) from the North Carolina Children's Hospital

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Categories: Autoimmune diseases | Gastroenterology

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